REMARKS

Claims 1-4, 7-9, 13, 19, 20, 31, 32, and 48-52 were pending in the application. Claim 1 has been amended, and claims 8, 13, 48, and 49 have been cancelled. Accordingly, upon entry of this amendment, claims 1-4, 7, 9, 19, 20, 31, 32, 50-52 will be pending and under examination. Support for the claim amendments may be found throughout the specification and claims as originally filed. In particular, Applicants submit that support for the amendments to claim 1 may be found, for example, in paragraphs [0026] and [0036]-[0038] as well as Figures 4a and 4b of the published application (US 2008/0025913). No new matter has been introduced.

Amendments and cancellations of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The amendments are solely being made to expedite prosecution of the present application. Applicants reserve the option to further prosecute the same or similar claims in the instant or subsequent application.

Applicants acknowledge with appreciation the indication in the office action that Applicants' Amendment filed on October 4, 2010 has overcome all previous rejections.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Claims Rejected Under 35 U.S.C. § 112, First Paragraph – Written Description

Claims 1-4, 7-9, 13, 19, 20, 31, 32, 48, and 50-52 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement for the introduction of new matter. The Examiner acknowledges that the instant application provides the polypeptides of SEQ ID NOS:10 and 18 in Figures 4a and 4b, respectively, and that the specification indicates that these polypeptides combine to form the "*IG4*" antibody V region (see page 3 of the office action). However, the Examiner alleges that the specification does not adequately describe an antibody defined only by the CDRs of the light and heavy chains of SEQ ID NOs:10 and 18, respectively.

Applicants respectfully disagree with the rejection. However, in an effort to expedite prosecution of the application, the claims have been amended, and the amendments are believed to obviate the rejection. Claim 1 has been amended to specify that the recited DC-SIGN antibodies are ***humanized*** antibodies. Accordingly, the claims are now directed to a genus of humanized DC-SIGN antibodies that comprises the light chain CDRs of SEQ ID NO:10 and the heavy chain CDRs of SEQ ID NO:18. Applicants submit that the currently pending claims are fully supported by the application as originally filed.

As described in the examples of the instant disclosure, Applicants used a genetic screening assay to identify several novel DC-SIGN antibodies from mouse IgG1 and IgG2a libraries (see, e.g., paragraphs [0083]-[0094] of the published application). The specification clearly provides the unique light chain (i.e., Figures 4a and 4c) and heavy chain (i.e., Figures 4b and 4c) amino acid sequences of mouse antibodies that specifically bind to human DC-SIGN (see, e.g., [0026], [0093], and [0094] of the published application). In particular, the specification provides the light chain (see, e.g., SEQ ID NO:10 of Figure 4a) and heavy chain (see, e.g., SEQ ID NO:18 of Figure 4b) amino acid sequences of the mouse DC-SIGN antibody *1G4*. Accordingly, the claims of the instant application are directed to antibodies that specifically bind to human DC-SIGN.

According to the instant disclosure, anti-DC-SIGN antibodies include polyclonal, monoclonal, chimeric and single chain antibodies, as well as fragments (e.g., Fab, Fv, scFv, and Fc fragments) and Fab expression libraries (see, e.g., paragraph [0031] of the published application). In particular, the specification clearly teaches that an "anti-DC-SIGN antibod[y] of the present disclosure can be a ***humanized*** antibody" (***emphasis added***) (see paragraph [0020] of the published application). With respect to humanized antibodies, the instant disclosure teaches that:

> "'[H]umanized' antibodies are those antibodies wherein amino acids outside the CDR are replaced with corresponding amino acids derived from human immunoglobulin molecules…Recombinant DNA technology can be used to produce a humanized antibody wherein the CDRs of a variable region of one immunoglobulin are replaced with the CDRs from an immunoglobulin with a different specificity such that the humanized antibody recognizes the desired target but is not recognized in a significant way by the human subject's immune system. Specifically, site directed mutagenesis is used to graft the CDRs onto the framework. Other approaches for humanizing antibodies are described in U.S. Pat. Nos. 5,585,089 and 5,693,761 and WO 90/07861. These antibodies have ***one or***

> ***more CDRs*** and additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin. Specifically, these patents describe the preparation of a ***humanized antibody that binds to a receptor by combining the CDRs of a mouse monoclonal antibody with human immunoglobulin framework and constant regions***. Human framework regions can be chosen to maximize homology with the mouse sequence. A computer model can be used to identify amino acids in the framework region which are likely to interact with the CDRs or the specific antigen and then mouse amino acids can be used at these positions to create the humanized antibody. In one embodiment, the antibody includes ***one or more CDR domains of the antibody***." (***emphasis added***) See paragraphs [0037]-[0038] of the published application.

Therefore, the specification clearly contemplates humanized antibodies in which the CDRs of the mouse monoclonal antibody (e.g., *1G4*) are inserted into a human immunoglobulin framework. As discussed in detail below, the skilled artisan, in view of the knowledge in the art at the time of filing, would have been able to readily identify the mouse CDRs in the disclosed light and heavy chain variable region sequences of the *1G4* antibody (i.e., SEQ ID NOs: 10 and 18, respectively) and clone these domains into a human antibody framework based on teachings of the application as originally filed. For example, the specification discloses the specific CDR3 sequences for several anti-DC-SIGN antibodies. In particular, the specification defines the heavy chain CDR3 sequence (i.e., SEQ ID NO:49) and the light chain CDR3 sequence (i.e., SEQ ID NO:45) of the *1G4* antibody (see, e.g., paragraphs [0038], [0094], and [0095] of the published application). Furthermore, originally filed claim 8 is directed to humanized anti-DC-SIGN antibodies that comprise the heavy and light chain CDR3 (i.e., SEQ ID NOs: 45 and 49, respectively) of the *1G4* antibody. Accordingly, Applicants submit that one of skill in the art would understand that specification clearly teaches humanized DC-SIGN antibodies that include the CDR domains of the *1G4* antibody.

Furthermore, in the analysis of whether the specification complies with the written description requirement, the examiner is required to compare the scope of the claims with the scope of the description to determine whether the applicant has demonstrated ***possession*** of the claimed invention. Applicants submit that possession may be demonstrated in many ways. For example, MPEP 2163.II.A. 3(a), paragraph 3 states that:

> An applicant may show possession of an invention by ***disclosure of drawings*** or structural chemical formulas that are sufficiently detailed to show that applicant

> was in possession of the claimed invention as a whole. See, e.g., *Vas-Cath*, 935 F.2d at 1565, 19 USPQ2d at 1118 ("drawings alone may provide a 'written description' of an invention as required by Sec. 112*); *In re Wolfensperger*, 302 F.2d 950, 133 USPQ 537 (CCPA 1962) (the drawings of applicant's specification provided sufficient written descriptive support for the claim limitation at issue); *Autogiro Co. of America v. United States*, 384 F.2d 391, 398, 155 USPQ 697, 703 (Ct. Cl. 1967); ... *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.... The description need only describe in detail that which is new or not conventional. See *Hybritech v. Monoclonal Antibodies*, 802 F.2d at 1384, 231 USPQ at 94; *Fonar Corp. v. General Electric Co.*, 107 F.3d at 1549, 41 USPQ2d at 1805.(***emphasis added***)

Therefore, possession may be demonstrated, for example, by a clear depiction of the invention in detailed drawings that permit a person skilled in the art to clearly recognize that the applicant had possession of the claimed invention. Applicants submit that the instant application clearly meets this standard for written description.

As described in detail above, the instant application provides the polypeptide sequences of the light and heavy chain variable regions (i.e., SEQ ID NOs:10 and 18, respectively) of the mouse antibody *1G4* (see, e.g., paragraphs [0026] and [0094]-[0095] as well as Figure 4a and 4b of the published application). Applicants submit that one of skill in the art would understand that the polypeptides of SEQ ID NOs:10 and 18 depicted in Figures 4a and 4b, respectively, ***necessarily*** contain all the CDRs of the *1G4* antibody. As indicated above, Applicants also assert that the specification clearly teaches humanized DC-SIGN antibodies and supports claims to a humanized antibody by reference to the CDRs of the mouse heavy and light chain variable regions. Accordingly, in view of the knowledge in the art at the time of filing, Applicants submit that Figures 4a (SEQ ID NO:10) and 4b (SEQ ID NO:18), combined with the teachings in the specification regarding humanized antibodies, clearly demonstrate that Applicants were in possession of the currently claimed invention.

Applicants further submit that the written description requirement must be applied in the context of the particular invention in view of the state of the knowledge in the art at the time of filing. For example, MPEP 2163.II.A. 3(a), paragraph 7 states that:

> What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94. >See also *Capon v. Eshhar*, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005). If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient").

Accordingly, Applicants submit that is not necessary that specification specifically define each of the six CDR sequences within the heavy and light chain variable regions of the *1G4* antibody as the skilled artisan, in view of the knowledge in the art, could readily identify these regions within SEQ ID NOs: 10 and 18.

At the time the instant application was filed, Applicants submit that methods for generating recombinant antibodies were well-known in the art and routine. In particular, since at least as early as 1991, the framework and CDR sequences of an antibody could be unambiguously determined and assigned using the Kabat numbering system. *See*, e.g., Kabat *et al.* (1991) "Sequences of Proteins of Immunological Interest." NIH Publication No. 91-3242, U.S. Department of Health and Human Services, Bethesda, MD ("Kabat *et al.*" cited in the Office Action Responses of December 29, 2009 and April 22, 2010). In particular, the Kabat *et al.* numbering system is a widely established method for assigning amino acid residues of an immunoglobulin molecule to a particular domain, such as a framework region (FR) or CDR. Specifically, Kabat *et al.* aligns 324 mouse kappa light chain group V sequences and 262 mouse heavy chain subgroup I(A) sequences and delineates each FR and CDR region for the heavy and light chains. *Supra* at pages 208-223 and 339-350. The alignments clearly show the delineation between the CDR regions and the FR regions of the antibodies, i.e., the CDRs are regions of high sequence variability interspersed between the well conserved framework regions. Accordingly, Applicants submit it was well within the purview of the skilled artisan to determine the position of CDRs within the light and heavy chain variable regions of antibody at the time of filing.

As indicated above, the specification clearly provides the CDR3 sequences for the light and heavy chain variable regions of the 1G4 antibody (i.e., SEQ ID NOs: 49 and 45, respectively). Based on the teachings of Kabat, Applicants submit that one of skill in the art could readily identify the framework regions in ***any antibody***, including the *1G4* antibody of the instant disclosure. Therefore, by using well-known methods in the art, the skilled artisan could identify CDRs 1 and 2 located within SEQ ID NOs:10 and 18 of the instant disclosure. For example, a comparison of the first-listed Kabat *et al.* heavy chain sequence on page 339 with the heavy chain sequence of antibody 1G4 (SEQ ID NO: 18) is shown below:

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...-FR1-- -CDR1- -----FR2------ ------CDR2------ -FR3-....KABAT (PAGE 339)
...TGDSIT         WIRKFPGNKLEYMG                 RISIT    KABAT (PAGE 339)
...TGYSIT SGYYWN WIRQSPGNKLEWMG YISTDGNSDYNPSFKN RISIT....SEQ ID NO: 18
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As shown in the alignment above, the borders of the FR regions as taught by Kabat *et al.* directly correspond to the borders of the framework regions of SEQ ID NO: 18. Therefore, it is readily apparent where regions FR1, CDR1, FR2, CDR2 and FR3 fall within SEQ ID NO: 18. By using the same technique, Applicants submit that the skilled artisan could also readily identify CDRs 1 and 2 located within SEQ ID NO:10. Accordingly, the identities of the heavy chain and light chain CDR regions for antibody 1G4 were clearly taught in the instant application by disclosing SEQ ID NOs: 10 and 18. Based on the teachings in the application regarding humanized antibodies, Applicants submit that one of skill in the art would readily be able to identify the mouse CDRs in the disclosed light and heavy chain variable region sequences of the *1G4* antibody (i.e., SEQ ID NOs: 10 and 18, respectively) and clone these domains into a human antibody framework.

In view of the above remarks, Applicants submit that the currently pending claims do not introduce new matter. Furthermore, Applicants assert that one of skill in the art would have understood that the application clearly supports the pending claims and that Applicants were in possession of the claimed invention. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above remarks, Applicants believe the pending application is in condition for allowance. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000.

Please charge our Deposit Account No. 18-1945 in the amount of $180.00 covering the fee set forth in 37 CFR 1.17(p). The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 18-1945, under Order No. ALEX-P01-112.

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Respectfully submitted,

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